PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

WRITTEN OPINION
(PCT Rule 66)

Date of mailing *(day/month/year)*	13.01.2004
Applicant's or agent's file reference: RIOY/P28304PC	**REPLY DUE** **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB 03/01625	15.04.2003	19.04.2002

International Patent Classification (IPC) or both national classification and IPC
A61K45/00

Applicant
IMPERIAL COLLEGE INNOVATIONS LIMITED et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 19.08.2004

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I. Basis of the opinion

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed")*:

Description, Pages

1-55 as originally filed

Claims, Numbers

1-36 as originally filed

Drawings, Sheets

1/6-6/6 as originally filed

Sequence listing part of the description, pages:

1-7, filed with the letter of 300703,

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   ☐ the language of publication of the international application (under Rule 48.3(b)).
   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.
   ☐ filed together with the international application in computer readable form.
   ☒ furnished subsequently to this Authority in written form.
   ☒ furnished subsequently to this Authority in computer readable form.
   ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:
   ☐ the claims, Nos.:
   ☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 35

   because:

   ☒ the said international application, or the said claims Nos. 35 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the Standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	see seperate sheet
Inventive step (IS)	Claims	see seperate sheet
Industrial applicability (IA)	Claims	see seperate sheet

2. Citations and explanations

   see separate sheet

Reference may be made to the following documents, as well as to documents cited in the application:

D1: CYTOKINE, vol. 12, no. 2, 2000, pages 165-170
D2: WO 02 090552
D3: METHODS IN ENZYMOLOGY, vol. 342, 2001, pages 10-20
D4: METHODS, vol. 15, 1998, pages 233-242
D5: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 280, 2001, pages 933-939
D6: WO 02 06343

Remarks under Article 5 and 6 PCT:

The present claims are considered so speculative and so unclearly defined that a complete examination is not possible, (see reasons given in the international search report).

The present application is based on the finding that OAS genotype is linked with the outcome of HCV infection and that patients who have a GG genotype at position 84 in the untranslated 3'end of exon 8 of OAS-1 are more likely to have persistent HCV infection in comparison to those with AG or AA genotype at the same position.

Thus, the present contribution to the art cannot be considered to commensurate with the scope of the present claims, since the present claims cover any compound which is able to "modulate" the level of activity of the OAS gene or enzyme, (excluding interferon or isoprenoids) for treating hepatitis C infection. It is not considered that the present application contribute with any teaching having regard to patients, who have any genotype other than the GG genotype at position 84 in the untranslated 3'end of exon 8 of OAS-1. It is also not considered that the application has demonstrated sufficient evidence that any substance, which is able to "modulate" the activity of the OAS gene or enzyme will result in the successful treatment of hepatitis C infection.

Corresponding objections are raised for the subject matter relating to compounds and methods comprising "compounds capable of modulating the activity of the RNAse L gene or enzyme.

Moreover, on present page 42 it is stated that "our data suggest that the 3'UTR SNP in OAS-1 is important in determining the natural outcome of HCV infection". This statement as well as the results reported from the study described on pages 32 ff. are considered to amount to the contribution to the art. However, this finding is not considered commensurate with the scope of the present claims, which all are directed to highly speculative subject matter, which stills needs to be investigated and confirmed. It has e.g. not even been demonstrated that the patients having the GG genotype will benefit from the exogenous delivery of the presently claimed "modulators". In fact, not even one example of a compound falling within the expressions "modulators of OAS gene/protein" or "modulators of RNAse L gene/protein" is given in the application, which again underlines the highly speculative nature of the presently claimed subject matter.

The presently claimed in-vitro screening methods have also not been performed and do not contribute to the art with anything novel or inventive, since the screening methods are all known, (cf. present example 2 and 3).

Section III
Non-establishment of opinion

Claim 35 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Section V
V.1. Novelty
Remarks under Article 33(2) PCT:

It is not considered feasible to examine the presently claimed subject matter in view of the provision of Article 33(2) EPC, since the claimed subject matter is considered so unsupported, insufficiently disclosed and speculative that the claimed subject matter does not fulfil the requirements of Articles 5 and 6 PCT.

It is however noted that present page 5, lines 9-23 reports on prior at studies, which have investigated the effects of OAS levels in patients infected with HCV. These

studies have not found a correlation between OAS levels and the successful treatment of hepatitis C. It can therefore not be considered that the present subject matter is directed to a novel treatment, because the presently claimed treatment has not been demonstrated to be any more effective than what is described in the mentioned passage describing prior art studies.

V.2. Inventive step

Remarks under Article 33(3) PCT:

An inventive step of the presently claimed subject matter cannot be assessed since no technical effects of the claimed subject matter have been demonstrated. It is also noted that it is state of the art that OAS has anti-viral properties, (see e.g. D5).

V.3 Industrial applicability

Remarks under Article 33(4) PCT:

For the assessment of the present claim 35 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

The other claims meet the requirements of Article 33(4) PCT.